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The Case | A boy with recurrent stones

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Figure 1 | Plain abdominal film at time of first presentation (2000): A small staghorn calculus obstructing the ureter and multiple stones within the renal pelvis.

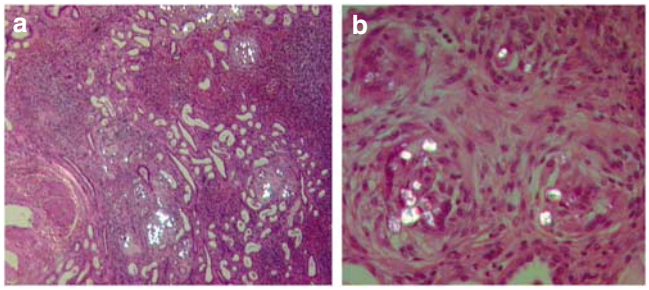

Figure 2 | Histology slides from nephrectomized kidney. (**a**) Cortical, periodic acid–Schiff-stained section of nephrectomized right kidney (original magnification ×40). (**b**) Enlarged area from panel (**a**) (original magnification ×400); periodic acid–Schiff.

A 16-year-old boy was referred with multiple episodes of nephrolithiasis since the age of 8 years. Plain abdominal film at first presentation revealed a small staghorn calculus obstructing the ureter and multiple stones within the right renal pelvis (Figure 1). The past medical, surgical and family history was unremarkable and the boy was not receiving any medication. He was referred to a hospital specialized in pediatric urology where extended nephropyelolithotomy with lower pole resection was performed. After the procedure, right-sided split renal function improved from 16 to 36%. Over the next 7 years, episodes of nephrolithiasis were initially confined to the right kidney for which he received in total 12 extracorporeal lithotripsy sessions and 2 open nephrolithotomies. In December 2004, his right kidney was found to be atrophic with 1.6% split function. At this time, stone formation had also been noted on the left side, and again was treated with extracorporeal lithotripsy. Before removal of the right kidney in 2006, a normal urinary calcium excretion was noted and the nephrectomy specimen was reported as 'an atrophic kidney with chronic interstitial nephritis'. We were subsequently able to review the pathology slides (Figure 2).

What do you see in the pathological specimen? What is your clinical diagnosis?

SEE NEXT PAGE FOR ANSWERS

The Diagnosis | Primary hyperoxaluria type II (PH II)

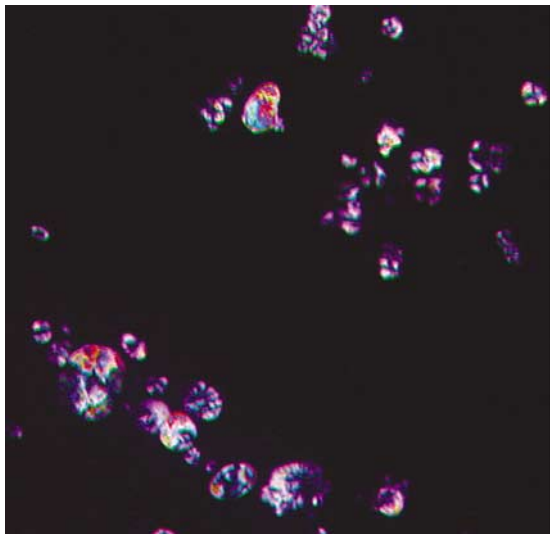

Figure 3 | Birefringent calcium oxalate aggregates by polarized light, some with a typical envelope structure.

Review of renal pathology specimens (Figure 2a) revealed chronic interstitial fibrosis, severe tubular atrophy/loss, and focal lymphoplasmacytic infiltrates. On high-power (Figure 2b) examination, tubular cross-sections revealed fragmented epithelial wall and obstructed lumina due to calcium oxalate deposits. The birefringent nature of the crystals can be easily seen in polarized light (Figure 3), which is suggestive of calcium oxalate, a remarkable finding however not reported by the consulted pathologist (Figure 2a and b). Hyperoxaluria of >1 mmol/1.73 m^2/day (normal <0.5) and L-glyceric aciduria of 662 mmol/mol creatinine (normal <32) were noted.

Metabolic disorders are the most common cause of urolithiasis in childhood. A history of frequent calculi should always raise suspicion of an underlying disease. Despite recurrent stones needing frequent interventions, proper evaluation had not been carried out in this case until it was late.

Two rare genetic forms of primary hyperoxaluria (PH) are currently known: PH type I is caused by absence of or low catalytic activity of liver-specific alanine-glyoxylate aminotransferase. PH type II is less common and is caused by defective glyoxylate reductase/hydroxypyruvate reductase (GRHPR). Clinical hallmarks in both are recurrent urolithiasis and/or progressive nephrocalcinosis; however, PH I has a more severe phenotype, with end-stage renal failure being the regular outcome.[1,2] A discriminator is the increased excretion of urinary glycolate in most patients with PH I, or L-glycerate in PH II.[3] A significant number of patients are diagnosed late or even only in end-stage renal failure.[4] Liver biopsy is still considered the gold standard for diagnosis, but mutational analysis has become increasingly reliable.[5] In our case diagnosis was established by a homozygous mutation (103delG) of the *GRHPR* gene.

Although unlikely in this case, PH has to be differentiated from the (more common) secondary causes. Therefore intestinal (hyper) absorption can be quantified by the $^{13}C_2$-oxalate absorption test (which in our case was 6.5%—well within normal limits).

Hydration and urine alkalization are still the backbone of conservative therapy. Pyridoxine treatment can be effective in PH I. Extensive stone removal procedures to the uncomplicated calculi should be avoided. Combined liver–kidney (PH I) or isolated kidney transplantation (PH II) are the treatments of choice in end-stage renal failure.

DISCLOSURE

All the authors declared no competing interests.

REFERENCES

1. Leumann E, Hoppe B. The primary hyperoxalurias. *J Am Soc Nephrol* 2001; **12**: 1986–1993.
2. Milliner DS, Wilson DM, Smith LH. Phenotypic expression of primary hyperoxaluria: comparative features of types I and II. *Kidney Int* 2001; **59**: 31–36.
3. Williams HE, Smith LH. L-Glyceric aciduria: a new genetic variant of primary hyperoxaluria. *N Engl J Med* 1968; **278**: 233–239.
4. Hoppe B, Latta K, von Schnakenburg C *et al.* Primary hyperoxaluria—the German experience. *Am J Nephrol* 2005; **25**: 276–281.
5. Webster KE, Ferree PM, Holmes RP *et al.* Identification of missense, nonsense, and deletion mutations in the GRHPR gene in patients with primary hyperoxaluria type II (PH2). *Hum Genet* 2000; **107**: 176–185.